

PCT

WORLD INTELLECTUAL PROPERTY ORGANIZATION  
International Bureau



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 7 : <b>A61K 7/16</b>		A1	(11) International Publication Number: <b>WO 00/69401</b> (43) International Publication Date: 23 November 2000 (23.11.00)
(21) International Application Number: PCT/US00/12972 (22) International Filing Date: 11 May 2000 (11.05.00)  (30) Priority Data: 09/312,287 14 May 1999 (14.05.99) US		(81) Designated States: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).  Published <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>	
(71) Applicant: COLGATE-PALMOLIVE COMPANY [US/US]; 300 Park Avenue, New York, NY 10022 (US).  (72) Inventors: YAMANE, Odete, T.; Rua Biobedas, 15 Apto., CEP-63 Saude S. Paulo, SP (BR). CORREA, Fernanda, C., G.; Rua Joaquim Guarani, CEP-0452 Brooklyn S. Paulo, SP (BR). MORISITA, Rosangela, Takako; Av. do Cafe, 54-Apto., CEP-151 Jabaquara S. Paulo, SP (BR).  (74) Agents: SHAPIRO, Paul et al.; Colgate-Palmolive Company, 909 River Road, P.O. Box 1343, Piscataway, NJ 08855-1343 (US).			
(54) Title: METHOD FOR THE MANUFACTURE OF TOOTHPASTE			
(57) Abstract			
<p>A method is disclosed for the manufacture of a toothpaste containing an ingredient mixture of a calcium carbonate abrasive, a thickener and an aqueous humectant wherein there is sequentially added the calcium carbonate abrasive dispersed in a high solids aqueous dispersion containing 50 to 80% by weight calcium carbonate to the aqueous humectant and thereafter adding the binder and binding the ingredients before any further ingredients are added to the mixture to produce the toothpaste.</p>			

**FOR THE PURPOSES OF INFORMATION ONLY**

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece			TR	Turkey
BG	Bulgaria	HU	Hungary	ML	Mali	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MN	Mongolia	UA	Ukraine
BR	Brazil	IL	Israel	MR	Mauritania	UG	Uganda
BY	Belarus	IS	Iceland	MW	Malawi	US	United States of America
CA	Canada	IT	Italy	MX	Mexico	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NE	Niger	VN	Viet Nam
CG	Congo	KE	Kenya	NL	Netherlands	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NO	Norway	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	NZ	New Zealand		
CM	Cameroon			PL	Poland		
CN	China	KR	Republic of Korea	PT	Portugal		
CU	Cuba	KZ	Kazakhstan	RO	Romania		
CZ	Czech Republic	LC	Saint Lucia	RU	Russian Federation		
DE	Germany	LI	Liechtenstein	SD	Sudan		
DK	Denmark	LK	Sri Lanka	SE	Sweden		
EE	Estonia	LR	Liberia	SG	Singapore		

## METHOD FOR THE MANUFACTURE OF TOOTHPASTE

### BACKGROUND OF THE INVENTION

5

#### 1. Field of the Invention

This invention relates to the manufacture of toothpastes and more particularly to a method of manufacturing a toothpaste which contains an abrasive system comprised at least in part of calcium carbonate.

10

#### 2. The Prior Art

Dentifrices, such as toothpaste are generally extrudable pastes containing insoluble abrasives that aid in the removal of plaque, stains and other deposits from the teeth and help to polish them. Toothpaste compositions contain a variety of ingredients, the major types of ingredients generally being abrasive particulates, a thickening agent, a liquid vehicle and surfactant. Other ingredients include flavoring agents and various other constituents for cosmetic, therapeutic or aesthetic effects.

20

Abrasives suitable for use in toothpaste compositions are generally finely divided, water-insoluble powdered materials such as silica, dicalcium phosphate dihydrate, calcium carbonate or calcined alumina. The toothpaste generally consists of a suspension of the abrasive in an aqueous humectant liquid phase. In order to hold the solid and liquid ingredients in the form of a stable paste with desirable rheological properties, the toothpaste invariably also includes a thickener or binder. A large number of different thickeners are known to the art and include, carboxymethylcellulose, xanthan gum, guar gum, carrageenan and mixtures thereof as thickener systems for toothpaste.

When preparing toothpastes, the toothpaste manufacturer encounters certain difficulties using abrasive powders and thickener systems to make a consumer acceptable toothpaste. For example, handling problems are encountered with the powdered abrasive where the particulate solids represent 10-60% by weight of the total toothpaste product and 5 wherein the powders are low in bulk density which causes powder loss on debagging and during addition to the ingredient mixing tank. Also, upon the addition of the abrasive powder to the other ingredients in the mixing tank, there is a strong tendency towards lumping when combined with the water and humectant liquids present therein

10

#### SUMMARY OF THE INVENTION

In accordance with the present invention, a method is provided for the rapid, lump-free addition of calcium carbonate abrasive powders used for the preparation of toothpaste compositions wherein the powders constitute a major portion of the product, which method is 15 a marked simplification of earlier powder addition techniques and comprises charging the water and humectant vehicle ingredients of the toothpaste to a mixing tank, introducing the abrasive calcium carbonate powder as a high solids slurry, in the order of 50-80% by weight solids, directly into the liquid vehicle and thereafter subjecting the ingredient mixture to homogenization by intimate mixing followed sequentially by the addition of a thickener and 20 additional water to adjust the rheology of the paste product to the desired extrudable consistency.

It is critical to the practice of the present invention that the thickener ingredient be added to the water/humectant liquid vehicle after the addition of the abrasive slurry as the 25 reverse sequence will cause a viscous gel to form which is difficult to subject to further processing. It is further critical to the method of the present invention that any further water addition to adjust the toothpaste rheology be made after the addition of the thickener so that a lump-free, smooth textured toothpaste product is obtained.

In a preferred embodiment of the invention, an essentially smooth, lump-free dentifrice paste is obtained in accordance with the above described method by first introducing a liquid vehicle comprised of a humectant such as glycerol, liquefied sorbitol

5       (generally a 70% aqueous solution) or other liquid polyols, followed in sequence by the addition of the calcium carbonate abrasive slurry, a thickener such as carboxymethylcellulose and then water to a mixing tank and thereafter subjecting the ingredients to a continuous vacuum and intimate mixing between each sequence to prepare a homogeneous paste mixture.

10

The liquid vehicle of the dentifrice paste products made in accordance with the present invention is generally a humectant/water mixture, and will generally be present in the final paste product in the range of from about 10 to 85% by weight, with from 30-70% being a preferred range for toothpastes. Humectants used in dentifrice formulations are well known

15       in the art and include glycerine, sorbitol, propylene glycol, polyethylene glycol, mannitol, polypropylene glycols, and mixtures thereof.

Stable aqueous calcium carbonate slurries used in the method of the present invention generally contain about 50 to about 80% by weight calcium carbonate. Such slurry materials

20       are available commercially and are widely used in the paper making industry; calcium carbonate being a pigment which is excellent in whiteness and has affinity for ink, gloss and printability.

Inorganic dispersants which may be used to stabilize the calcium carbonate slurry

25       include such condensed phosphates as pyrophosphates, tripolyphosphates, trimetaphosphates, tetrametaphosphates, and hexametaphosphates, zinc salts and silicates. Organic dispersants, include polycarboxylates such as polyacrylates, polymethacrylates, and polymaleates and polyvinyl alcohol. Such dispersants are known to the art, for example, US 4,818,783 discloses dispersing calcium carbonate in an aqueous medium containing as the dispersant (1)

30       0.1 to 2 parts by weight of (a) a carboxyl group-containing water-soluble polymer possessing a number average molecular weight in the range of 2,000 to 80,000 and (b) a water soluble

condensed phosphate and (2) 0.03 to 1 part by weight of a water soluble anionic modified polyvinyl alcohol respectively based on 100 parts by weight of the calcium carbonate.

The content of calcium carbonate abrasive in the final paste product will range from  
5 about 20 to about 75% and preferably about 30 to about 60% by weight.

Thickeners that can be used in accordance with the method of the present invention  
preferably include the natural and synthetic gums and gum-like materials, desirably carboxyl  
methyl cellulose sodium carboxymethylcellulose, hydroxyethylcarboxymethylcellulose,  
10 carrageenin, gum tragacanth, xanthan gum, guar gum, alginates, bentonite and other natural  
clays and synthetic inorganic clays. The gums are hydratable or gelled with water or alkanols,  
especially with polyhydric alcohols such as glycerol and sorbitol.

The proportions of thickeners present in the toothpaste product of the present  
15 invention will generally be in the range of from 0.1 to about 5% by weight of the final  
product and in the case of synthetic gums such as sodium carboxymethylcellulose, the range  
will preferably be from about 0.1 to 3%.

Inorganic thickening agents suitable for use in the present invention include colloidal  
20 silicas having bodying properties, such as the aerogels Syloid 244 and 266 (available from W.  
R. Grace Company), Aerosil (available from DeGussa Co.) and pyrogenic silicas sold under  
the tradename Cab-O-Sils (available from Cabot Corporation). Tixosil 333 and Tixosil 43B  
(available from Rhodia Ltda.), Zeodent 165 (available from J.M. Huber Corporation).

25 In the manufacture of the toothpaste in accordance with the method of the present  
invention, mixing of the ingredients is accomplished in mixing vessels conventionally used  
and equipped for the manufacture of toothpaste. The ingredients may be charged to mixer at  
an elevated temperatures for example 45 to 70°C, but is preferably performed at room  
temperature to save heating and cooling times.

30

Once the homogeneous paste containing the aqueous humectant, abrasive and thickener is prepared, which can generally be referred to as a base paste, various other classes of ingredients may be added to finalize the toothpaste product, which additional ingredients generally include surfactants, silica aerogels or other colloidal silicas, therapeutic agents, preservatives and flavoring agents or other ingredients that will finalize the desired toothpaste product.

Examples of surfactants useful in the toothpastes prepared in accordance with the method of the present invention include anionic surfactants such as sodium alkylsulfates (sodium laurylsulfate, sodium myristylsulfate), sodium N-acylsarcosinates (sodium N-lauroylsarcosinate, sodium N-myristoylsarcosinate, N-acylglutamic acid salts (sodium N-palmitoylglutamate, etc.), and sulfosuccinic acid surfactants (polyoxyethylene alkyl disodium sulfosuccinate, dialkyl sodium sulfosuccinate).

Examples of nonionic surfactants usable in the method of the present invention include sugar fatty acid esters (sucrose fatty acid ester, maltose fatty acid ester, lactose fatty acid ester, etc.), polyoxyethylene alkyl ethers, polyoxyethylene sorbitan fatty acid esters (polyoxyethylene sorbitan mono laurate, polyoxyethylene sorbitan monostearate, etc.), polyoxyethylene fatty acid esters (polyoxyethylene-hardened castor oil, etc.), sorbitan fatty acid esters, fatty acid monoglycerides and polyoxyethylene/polyoxypolypropylene block copolymers.

Examples of amphoteric surfactants usable herein include N-alkyldiaminoethylglycine (N-lauryldiaminoethylglycine, N-myristyldiethylglycine, etc.), N-alkyl-N-carboxymethylammonium betaine, 2-alkyl-1-hydroxyethylimidazoline betaine sodium and lauryldimethylaminoacetic acid betaine.

Either one of the above described surfactants or a mixture of two or more thereof may be used to prepare the toothpaste composition of the present invention at a concentration ranging from 0.1 to 10% by weight based on the whole composition.

The toothpaste compositions prepared in accordance with the process of the present invention may also contain flavors such as menthol, arvensis mint oil, synthetic mint flavors, carvone, eugenol, methyleugenol, methyl salicylate, methyl eugenol, thymol, anethole, limonene, ocimene, n-decyl alcohol, citronellol, alpha-terpineol, linalol, ethyllinalol, vanillin, thyme, nutmeg, spearmint oil, peppermint oil, lemon oil, orange oil, sage oil, rosemary oil, cinnamon oil, winter green oil, clove oil and eucalyptus oil. Either one of these flavors or a mixture of two or more thereof may be used. The content thereof ranges from 0.1 to 5% by weight, preferably from 0.5 to 2% by weight, based on the whole composition.

The toothpaste compositions of the present invention may also contain sweeteners such as saccharin sodium, acesulfame potassium, glycyrrhizin, perillartine, thaumatin, aspartylphenylalanyl methyl ester and xylitol. The content of the sweeteners ranges from 0.01 to 1% by weight, preferably from 0.05 to 0.5% by weight, based on the whole composition.

The toothpaste composition prepared in accordance with the method of the present invention may furthermore contain therapeutic ingredients such as water-insoluble noncationic antibacterial agents such as triclosan, Vitamin E analogs (dl-.alpha.-tocopherol acetate, tocopherol succinate, tocopherol nicotinate, etc.), Vitamin A (retinol, alpha carotene, beta carotene), Vitamin B (B1-thyamin, B2-riboflavine, B3-niacine, B5-pantothenic acid, B6-piryodoxine, B7-biotine, B8/B9/Bc-folic acid, B12-cianocobalamine), Vitamin C (ascorbic acid, sodium ascorbate), cationic antibacterial agents (chlorhexidine hydrochloride, cetylpyridinium chloride), enzymes (dextranase, amylase, protease, mutanase, lysozyme), herbal extracts/oils (chamomile, myrrh, eugenol, tea tree oil, sage oil, mallow, eucalyptus, melissa, pomegranade, apricot, millefolium extract, tangerine extract), natural ingredients (algae, propolis), anticavity alkali metal agents and monofluorophosphates (sodium monofluorophosphate, potassium monofluorophosphate, etc.), fluorides (sodium fluoride, stannous fluoride, etc.), whitening agents (aluminum oxide, calcium peroxide), debriding agent (sodium bicarbonate), astringent salts (such as zinc), chlorophyll, and preservatives

such as methyl paraben, tooth desensitizing agents such as potassium and strontium salts, condensed antitartar phosphates such as sodium and potassium tetrapyrophosphate, pigments (Blue 15-CI74160, Green 7-CI74260, Red 4-CI12085, Yellow 115 CI47005:1), dyes (Red 40 CI16035, Red 33 CI17200, Red 3 CI45430, Carmine 5 CI75470, Blue 1 CI42090, Yellow 5 5 CI19140, Yellow 10 CI47005) Mica and Speckles. Use can be made of either one of these ingredients or a mixture of two or more thereof in amounts ranging from 0.001 to about 15% by weight of the toothpaste.

10

The following Example is illustrative of the invention. All percentages are by weight.

**Example**

A toothpaste was made according to the following formula:

15

	% Weight
Sorbitol	20.00
Carboxymethylcellulose (CMC)	1.20
Irradiated water	5.020
Calcium carbonate (65% by weight slurry)	63.080
Sodium saccharin	0.200
Methylparaben	0.100
Ethyl alcohol	1.500
Sodium silicate	1.000
Sodium monofluorophosphate	1.140
Sodium lauryl sulfate (SLS) 29% solution	5.600
Flavor	1.160

The toothpaste was made in Frima Mixer toothpaste mixer. Mixing was carried out under vacuum of 600-680 mm Hg. The mixing steps were as follows:

- Stage 1 - The sorbitol was put in the mixer.
- Stage 2 - Half the water content was added to the mixer.
- Stage 3 - The calcium carbonate slurry, containing 65% by weight calcium carbonate,  
5 available from Quimbarra Company, Rio de Janeiro, Brazil stabilized with sodium silicate and sodium hexametaphosphate dispersants was drawn into the mixer. Mixing took place for about 1 minute to prepare a homogeneous dispersion.
- Stage 4 - A suspension of CMC thickener and the preservative, methyl paraben in ethanol prepared in a separate mixing vessel, was added to the mixer and mixed for 15 minutes,  
10 with a mixing anchor speed of 22 rpm.
- Stage 5 - A solution of sodium saccharin and sodium monofluorophosphate was prepared with the remainder of the water in a separate vessel and added to the mixer and mixed for 2 minutes to produce a smooth cream.
- Stage 6 - Sodium silicate was added to the mixer.
- 15 • Stage 7 - The flavor was added to the mixer and mixed for 2 minutes.
- Stage 8 - SLS was added and mixed for 20 minutes.

The toothpaste prepared in accordance with the sequential steps described above had a satisfactory smooth texture and acceptable appearance. A comparative toothpaste, which  
20 was not made by the method of this invention, that is Stage 4, was performed before Stage 3 or Stage 5 was performed before Stage 4, resulted in a toothpaste product that had a rough granular texture. The coarse texture of the toothpaste ribbon, especially noticeable when spread with the finger, meant that the product was of poor quality. The toothpaste ribbon lacked the uniformly smooth texture required of an acceptable commercial product.

**CLAIMS****What is claimed is:**

5

1. A method for making a toothpaste containing an ingredient mixture of a calcium carbonate abrasive, a thickener and an aqueous humectant which comprises sequentially adding the calcium carbonate abrasive dispersed in a high solids aqueous dispersion containing about 50 to about 80% by weight calcium carbonate to the aqueous humectant and thereafter adding the thickener and mixing the ingredients before any further ingredients are added to the mixture to produce the toothpaste.
  2. The method of claim 1 wherein the thickener is carboxymethyl cellulose.
- 10
- 15 3. The method of claim 1 wherein the humectant is sorbitol.
  4. The method of claim 1 wherein the content of calcium carbonate in the toothpaste ranges from about 20 to about 70% by weight.
- 20
5. The method of claim 1 wherein the thickener is present in the toothpaste at a concentration of about 0.1 to about 5% by weight.

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/12972

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC 7 A61K7/16

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

WPI Data, PAJ, EPO-Internal, CHEM ABS Data

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	GB 1 599 689 A (COLGATE-PALMOLIVE) 7 October 1981 (1981-10-07) the whole document ----	1-5
A	EP 0 097 476 A (PROCTER & GAMBLE) 4 January 1984 (1984-01-04) example 1 ----	1-5
A	EP 0 565 401 A (COLGATE-PALMOLIVE) 13 October 1993 (1993-10-13) the whole document ----	1-5
A	EP 0 190 762 A (BLENDAX-WERKE R. SCHNEIDER) 13 August 1986 (1986-08-13) the whole document -----	1-5

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

\* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

\*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

\*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

\*&\* document member of the same patent family

Date of the actual completion of the international search

3 October 2000

Date of mailing of the international search report

11/10/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patenttaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl.  
Fax: (+31-70) 340-3016

Authorized officer

Fischer, J.P.

**INTERNATIONAL SEARCH REPORT**

Information on patent family members

International Application No

PCT/US 00/12972

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
GB 1599689	A 07-10-1981	AR	218540 A	13-06-1980
		AT	363602 B	25-08-1981
		AT	347279 A	15-01-1981
		AU	523563 B	05-08-1982
		AU	4611179 A	29-11-1979
		BE	876425 A	17-09-1979
		BR	7903126 A	11-12-1979
		CA	1118360 A	16-02-1982
		CH	641955 A	30-03-1984
		DE	2918132 A	29-11-1979
		DK	178579 A,B	26-11-1979
		FR	2426458 A	21-12-1979
		IE	48240 B	14-11-1984
		IT	1116852 B	10-02-1986
		JP	1449040 C	11-07-1988
		JP	54157843 A	13-12-1979
		JP	62056125 B	24-11-1987
		MX	153894 A	11-02-1987
		MY	10183 A	31-12-1983
		MY	10283 A	31-12-1983
		NL	7903191 A	27-11-1979
		NO	791702 A,B,	27-11-1979
		NZ	190071 A	16-03-1981
		PH	15533 A	09-02-1983
		PT	69497 A	01-05-1979
		SE	444763 B	12-05-1986
		SE	7902993 A	26-11-1979
		ZA	7901715 A	26-11-1980
EP 97476	A 04-01-1984	AT	46262 T	15-09-1989
		AT	66587 T	15-09-1991
		AT	66588 T	15-09-1991
		AT	60901 T	15-03-1991
		CA	1233121 A	23-02-1988
		DE	3380553 D	19-10-1989
		DE	3382169 D	28-03-1991
		DE	3382395 A	02-10-1991
		DE	3382396 A	02-10-1991
		EP	0297211 A	04-01-1989
		EP	0297212 A	04-01-1989
		EP	0297213 A	04-01-1989
		EP	0319516 A	07-06-1989
		EP	0345821 A	13-12-1989
		EP	0395117 A	31-10-1990
		FI	832275 A,B,	23-12-1983
		FI	88107 B	31-12-1992
		GR	79211 A	22-10-1984
		IE	56956 B	12-02-1992
		IE	56957 B	12-02-1992
		JP	6002657 B	12-01-1994
		JP	59042311 A	08-03-1984
		MX	156152 A	19-07-1988
		PH	22221 A	28-06-1988
		US	4806339 A	21-02-1989
		US	4772461 A	20-09-1988
		US	4885155 A	05-12-1989
		US	4999184 A	12-03-1991
		US	4515772 A	07-05-1985

**INTERNATIONAL SEARCH REPORT**

Information on patent family members

International Application No

PCT/US 00/12972

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
EP 97476	A	US	4590066 A	20-05-1986
		US	4684518 A	04-08-1987
EP 565401	A	13-10-1993	US 5236696 A AT 154512 T AU 3541793 A BG 61675 B BG 97579 A BR 9301305 A CN 1083700 A, B DE 69311616 D GR 93100121 A, B HK 1007282 A JP 6009335 A MX 9301514 A PL 298264 A RO 112988 A TR 28582 A US 5320832 A ZA 9301728 A ZW 3893 A	17-08-1993 15-07-1997 30-09-1993 31-03-1998 31-03-1995 05-10-1993 16-03-1994 24-07-1997 30-11-1993 09-04-1999 18-01-1994 01-12-1993 07-03-1994 30-03-1998 22-10-1996 14-06-1994 10-09-1994 11-01-1993
EP 190762	A	13-08-1986	DE 3504178 A AT 74747 T CH 672065 A DE 3684794 A JP 2118055 C JP 8032619 B JP 61183215 A ZA 8600599 A	14-08-1986 15-05-1992 31-10-1989 21-05-1992 06-12-1996 29-03-1996 15-08-1986 29-10-1986